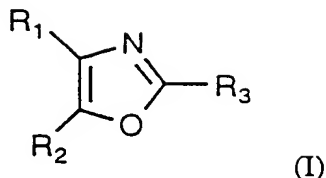


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What is claimed is:

1. A compound of the formula:



wherein:

R₁ and R₂ are independently selected from an optionally substituted aryl or heteroaryl group, provided that at least one of R₁ and R₂ is an optionally substituted heteroaryl, and further provided that both R₁ and R₂ are not the same heteroaryl group;

wherein when one of R₁ and R₂ is an optionally substituted aryl ring, the ring is substituted by one or two substituents, each of which is independently selected, and which, for a 4-phenyl, 4-naphth-1-yl or 5-naphth-2-yl substituent, is halo, cyano, -C(Z)NR₇R₁₇, -C(Z)OR₂₃, -(CR₁₀R₂₀)_m COR₃₆, -SR₅, -SOR₅, -OR₃₆, halo-substituted-C₁₋₄ alkyl, C₁₋₄ alkyl, -ZC(Z)R₃₆, -NR₁₀C(Z)R₂₃, or -(CR₁₀R₂₀)_mNR₁₀R₂₀;

and which, for other positions of substitution, is halo, -(CR₁₀R₂₀)_m-cyano, -C(Z)NR₁₆R₂₆, -C(Z)OR₈, -(CR₁₀R₂₀)_m COR₈, -(CR₁₀R₂₀)_m S(O)_mR₈, -(CR₁₀R₂₀)_m OR₈, halo-substituted-C₁₋₄ alkyl, -C₁₋₄ alkyl, -(CR₁₀R₂₀)_m NR₁₀C(Z)R₈, -(CR₁₀R₂₀)_m NR₁₀S(O)_m R₁₁, -(CR₁₀R₂₀)_m NR₁₀S(O)_m NR₇R₁₇, -(CR₁₀R₂₀)_m ZC(Z)R₈ or -(CR₁₀R₂₀)_m NR₁₆R₂₆;

and when one of R₁ and R₂ is an optionally substituted heteroaryl group, the substituent groups include one or two substituents each of which is independently selected from C₁₋₄ alkyl, halo, C₁₋₄ alkoxy, C₁₋₄ alkylthio, NR₁₀R₂₀, or an N-heterocyclyl ring which ring has from 5 to 7 members and optionally contains an additional heteroatom selected from oxygen, sulfur or NR₂₂;

R₃ is -X_aP(Z)(X_bR₁₃)₂, X_c or -(CR₁₀R₂₀)_n R₄;

R₄ is Q-(Y₁)_t;

Q is an aryl or heteroaryl group;

X_c is hydrogen, -(CR₁₀R₂₀)_n (Y₂)_p, -(CR₁₀R₂₀)_n -C=C- (CR₁₀R₂₀)_n (Y₂)_p, -(CR₁₀R₂₀)_n -C≡C- (CR₁₀R₂₀)_n (Y₂)_p, or halosubstituted C₁₋₁₀ alkyl;

t is an integer having a value of 1 to 3;

p is 0 or an integer having a value of 1, provided that when p is 0 then Y₂ is hydrogen;

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- X_a is -NR₈-, -O-, -S- or a C₁₋₁₀ alkylene chain optionally substituted by C₁₋₄ alkyl and optionally interrupted by -NR₈-, -O- or -S-;
- X_b is independently selected from -(CR₁₀R₂₀)_n, -NR₈-, -O- or -S-;
- Z is oxygen or sulfur;
- 5 n is 0 or an integer having a value of 1 to 10;
 n' is an integer having a value of 1 to 10;
 m is 0, or the integer 1 or 2;
 m' is 1 or 2;
 m'' is 0 or an integer having a value of 1 to 5;
- 10 Y₁ is independently selected from hydrogen, C₁₋₅ alkyl, halo-substituted C₁₋₅ alkyl, halogen, -X_a-P(Z)-(X_bR₁₃)₂ or -(CR₁₀R₂₀)_nY₂;
- Y₂ is halogen, -OR₈, -NO₂, -S(O)_m'R₁₁, -SR₈, -S(O)_m'NR₈R₉, -NR₈R₉,
 -O(CR₁₀R₂₀)_n'NR₈R₉, -C(O)R₈, -CO₂R₈, -CO₂(CR₁₀R₂₀)_n'CONR₈R₉,
 -ZC(O)R₈, -CN, -C(Z)NR₈R₉, -NR₁₀C(Z)R₈, -C(Z)NR₈OR₉, -NR₁₀C(Z)NR₈R₉,
15 -NR₁₀S(O)_m'R₁₁, -N(OR₂₁)C(Z)NR₈R₉, -N(OR₂₁)C(Z)R₈, -C(=NOR₂₁)R₈,
 -NR₁₀C(=NR₁₅)SR₁₁, -NR₁₀C(=NR₁₅)NR₈R₉, -NR₁₀C(=CR₁₄R₂₄)SR₁₁,
 -NR₁₀C(=CR₁₄R₂₄)NR₈R₉, -NR₁₀C(O)C(O)NR₈R₉, -NR₁₀C(O)C(O)OR₁₀,
 -C(=NR₁₃)NR₈R₉, -C(=NOR₁₃)NR₈R₉, -C(=NR₁₃)ZR₁₁, -OC(Z)NR₈R₉,
 -NR₁₀S(O)₂CF₃, -NR₁₀C(Z)OR₁₀, 5-(R₁₈)-1,2,4-oxadiazol-3-yl or 4-(R₁₂)-5-
20 (R₁₈R₁₉)-4,5-dihydro-1,2,4-oxadiazol-3-yl;
- R₅ is hydrogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl or NR₇R₁₇, excluding the moieties
 -SR₅ being -SNR₇R₁₇ and -SOR₅ being -SOH;
- R₆ is C₁₋₄ alkyl, halo-substituted-C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl or C₃₋₅
 cycloalkyl;
- 25 R₇ and R₁₇ is each independently selected from hydrogen or C₁₋₄ alkyl or R₇ and R₁₇
 together with the nitrogen to which they are attached form a heterocyclic ring of 5 to 7
 members which ring optionally contains an additional heteroatom selected from
 oxygen, sulfur or NR₂₂;
- R₈ is hydrogen, heterocyclyl, heterocyclalkyl or R₁₁;
- 30 R₉ is hydrogen, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, C₂₋₁₀ alkynyl, C₃₋₇ cycloalkyl, C₅₋₇
 cycloalkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl or R₈ and R₉ may together
 with the nitrogen to which they are attached form a heterocyclic ring of 5 to 7 members
 which ring optionally contains an additional heteroatom selected from oxygen, sulfur or
 NR₁₂;
- 35 R₁₀ and R₂₀ is each independently selected from hydrogen or C₁₋₄ alkyl;
- R₁₁ is C₁₋₁₀ alkyl, halo-substituted C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, C₂₋₁₀ alkynyl, C₃₋₇
 cycloalkyl, C₅₋₇ cycloalkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;

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- R₁₂ is hydrogen, -C(Z)R₁₃ or optionally substituted C₁₋₄ alkyl, optionally substituted aryl or optionally substituted aryl-C₁₋₄ alkyl;
R₁₃ is hydrogen, C₁₋₁₀ alkyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;
- 5 R₁₄ and R₂₄ is each independently selected from hydrogen, alkyl, nitro or cyano;
R₁₅ is hydrogen, cyano, C₁₋₄ alkyl, C₃₋₇ cycloalkyl or aryl;
R₁₆ and R₂₆ is each independently selected from hydrogen or optionally substituted C₁₋₄ alkyl, optionally substituted aryl or optionally substituted aryl-C₁₋₄ alkyl, or together with the nitrogen which they are attached form a heterocyclic ring of 5 to 7 members
10 which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR₁₂ ;
R₁₈ and R₁₉ is each independently selected from hydrogen, C₁₋₄ alkyl, substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl or together R₁₈ and R₁₉ denote a oxygen or sulfur;
- 15 R₂₁ is hydrogen, a pharmaceutically acceptable cation, C₁₋₁₀ alkyl, C₃₋₇ cycloalkyl, aryl, aryl C₁₋₄ alkyl, heteroaryl, heteroarylalkyl, heterocyclyl, aroyl, or C₁₋₁₀ alkanoyl;
R₂₂ is R₁₀ or C(Z)-C₁₋₄ alkyl;
R₂₃ is C₁₋₄ alkyl, halo-substituted-C₁₋₄ alkyl, or C₃₋₅ cycloalkyl;
R₃₆ is hydrogen or R₂₃;
- 20 or a pharmaceutically acceptable salt thereof.
2. The compound according to Claim 1 wherein R₁ or R₂ is an optionally substituted 4-pyridyl or 4-pyrimidinyl.
- 25 3. The compound according to Claim 2 wherein the optional substituent is C₁₋₄ alkyl or NR₁₀R₂₀.
4. The compound according to any of Claims 1 to 3 wherein R₁ or R₂ is an optionally substituted phenyl.
- 30 5. The compound according to Claim 4 wherein the one or more optional substituents are independently selected from halogen or methoxy.
6. The compound according to any of Claims 1 to 5 wherein R₃ is X_C or
35 -(CR₁₀R₂₀)_nR₄.

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7. The compound according to Claim 6 wherein R₃ is hydrogen, -(CR₁₀R₂₀)_n(Y₂)_p, -(CR₁₀R₂₀)_n CH₃; and Y₂ is -NR₈R₉ or -NR₁₀C(Z)R₈; and R₄ is an optionally substituted phenyl.
- 5 8. The compound according to Claim 5 or 6 wherein R₃ is hydrogen, methyl, amino, -NR₁₀C(O)R₈, phenyl, or phenyl substituted by -SR₈ or -S(O)_mR₁₁.
9. The compound according to Claim 1 which is:
5-(3-Methoxyphenyl)-2-methyl-4-(4-pyridyl)oxazole;
10 5-(4-Fluorophenyl)-2-methyl-4-(4-pyridyl)oxazole;
2-Methyl-4-(Phenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-methyl-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-phenyl-5-(4-pyridyl)oxazole;
2-Amino-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole.
15 4-(4-Fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-methylpyrid-4-yl)oxazole;
4-(3,4-Dichlorophenyl)-5-(4-pyridyl)oxazole;
4-(3-Chlorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-(4-methylthiophenyl)-5-(4-pyridyl)oxazole;
20 4-(4-Fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-5-(4-pyridyl)oxazole;
2-Acetamido-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-amino-pyrimidin-4-yl)oxazole; or pharmaceutically acceptable salts thereof.
- 25 10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound according to any of Claims 1 to 9.
11. A method of treating a cytokine mediated disease in an animal in need thereof which method comprises administering to said animal an effective cytokine mediating
30 amount of a compound according to any of Claims 1 to 9.
12. The method according to Claim 11 wherein the cytokine mediated disease is asthma, adult respiratory distress syndrome, stroke, bone reabsorption diseases, arthritic joint conditions, and other inflammatory diseases.
- 35 13. The method according to Claim 11 or 12 wherein the compound is 5-(3-Methoxyphenyl)-2-methyl-4-(4-pyridyl)oxazole;

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- 5-(4-Fluorophenyl)-2-methyl-4-(4-pyridyl)oxazole;
2-Methyl-4-(Phenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-methyl-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-phenyl-5-(4-pyridyl)oxazole;
5 2-Amino-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-methylpyrid-4-yl)oxazole;
4-(3,4-Dichlorophenyl)-5-(4-pyridyl)oxazole;
4-(3-Chlorophenyl)-5-(4-pyridyl)oxazole;
10 4-(4-Fluorophenyl)-2-(4-methylthiophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-5-(4-pyridyl)oxazole;
2-Acetamido-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-amino-pyrimidin-4-yl)oxazole; or pharmaceutically acceptable
salts thereof.
- 15 14. The method according to any of Claims 11 to 13 wherein the mediation of the
disease state is by Interleukin-1 (IL-1).
- 20 15. The method according to any of Claims 11 to 13 wherein the mediation of the
disease state is by Tumor Necrosis Factor (TNF).
16. A method of treating inflammation in a mammal in need thereof which comprises
administering to said mammal an effective amount of a compound according to any of
Claims 1 to 9.